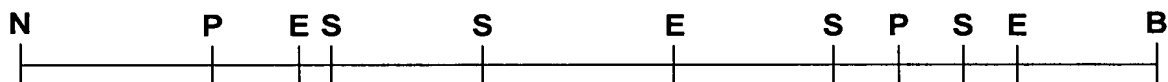


REPLACEMENT SHEET
Title: CLONING, OVEREXPRESSION AND
THERAPEUTIC USE...
Appl. No.: 09/833,745
Inventors: Joseph ROBERTS *et al.*
Atty. Docket No. 078728-0106

Figure 1: Restriction pattern of the HAL coding region cut with selected enzymes.

HAL



N - NdeI site introduced at the N-terminus

B - BamHI site introduced at the C-terminus

E - EagI

P - PstI

S - SphI

Figure 2: Experimentally derived peptide sequences of HAL

N-terminal

(M)ASAPQITLGLSGATAD

Internal

(M)ALADLDELLDEA

(M)GEPVEREVLRA

Figure 3: SphI digestion pattern of HAL gene showing oligonucleotide and subclones.

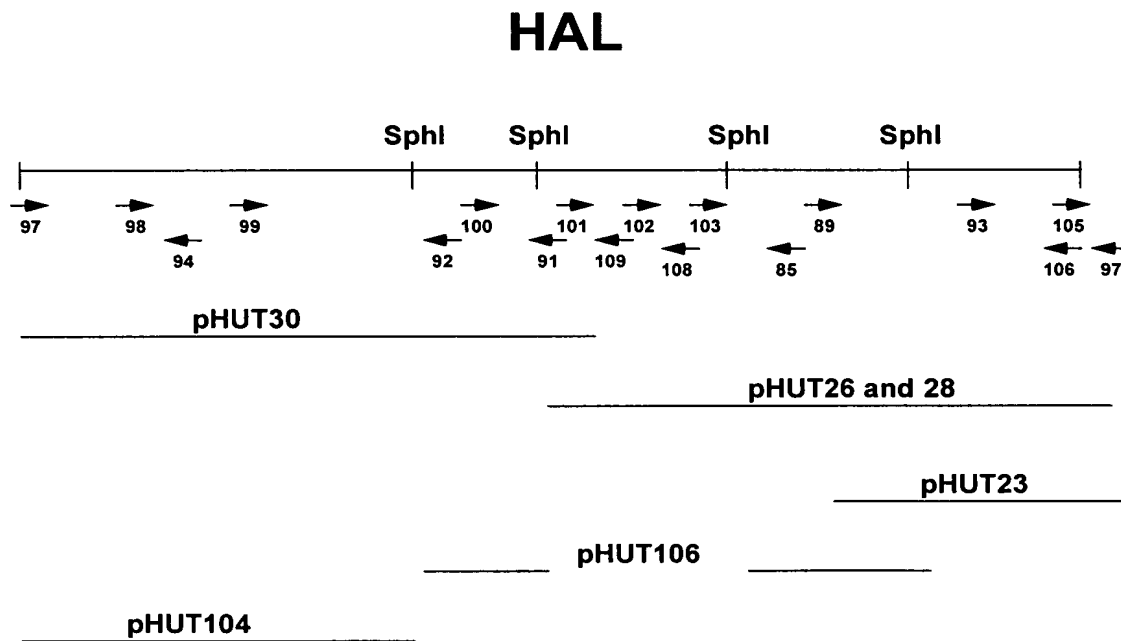
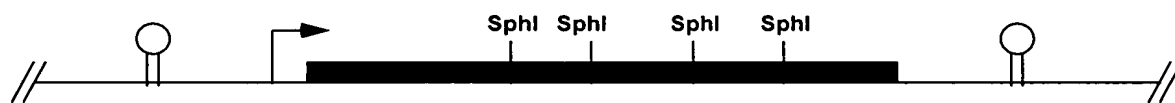


Figure 4: Histidine ammonia lyase overexpressing plasmid.

pHUT102



— ADI coding region

└─▶ T7 Promoter

○ Transcriptional Terminator

Figure 5: SDS-PAGE showing expression of HAL in *E. coli*.

Lanes: 1 2 3 4

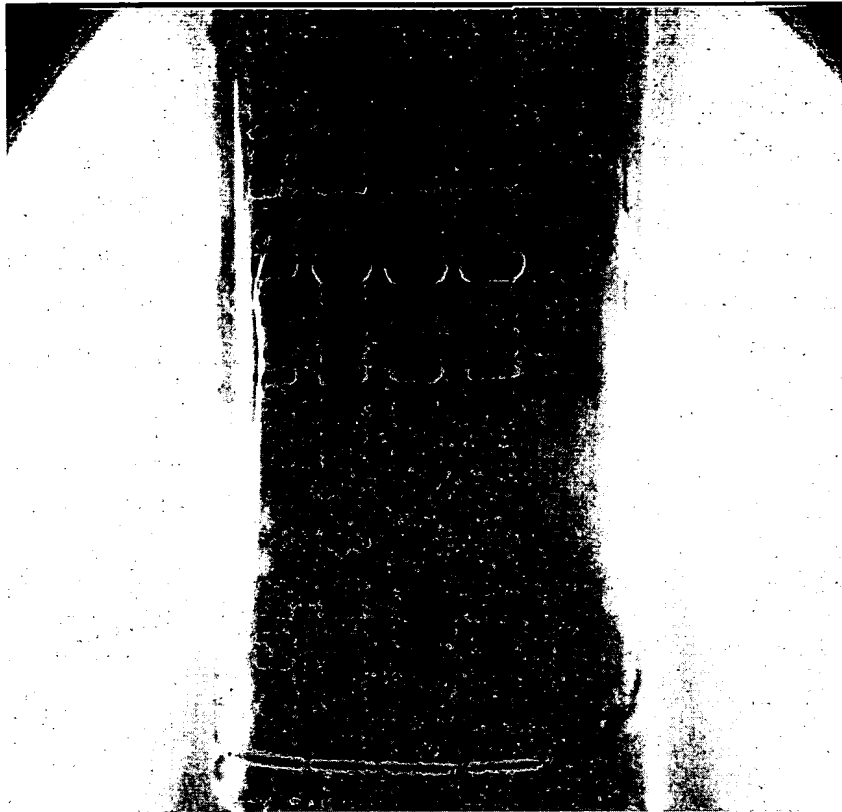


Figure 6: SDS-PAGE showing purification of HAL from *E. coli*

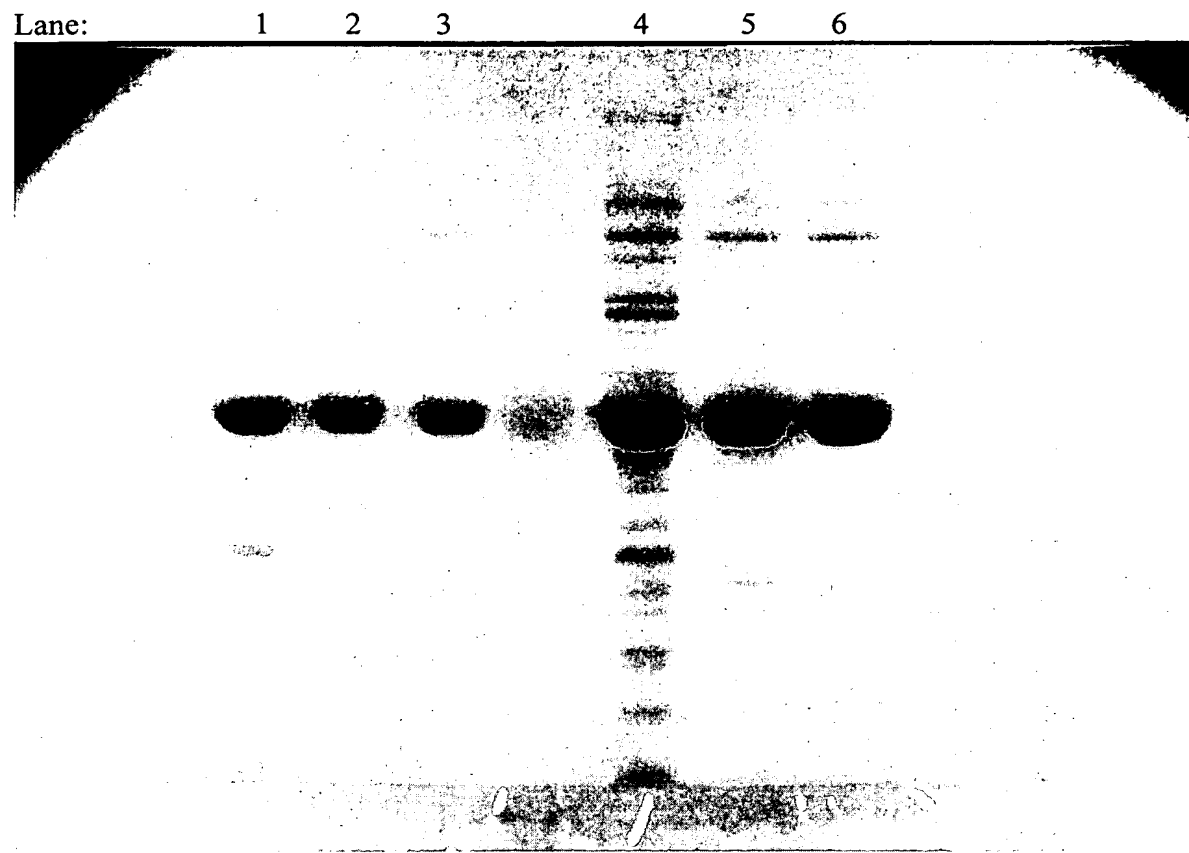


Figure 7: Effect of Temperature on HAL

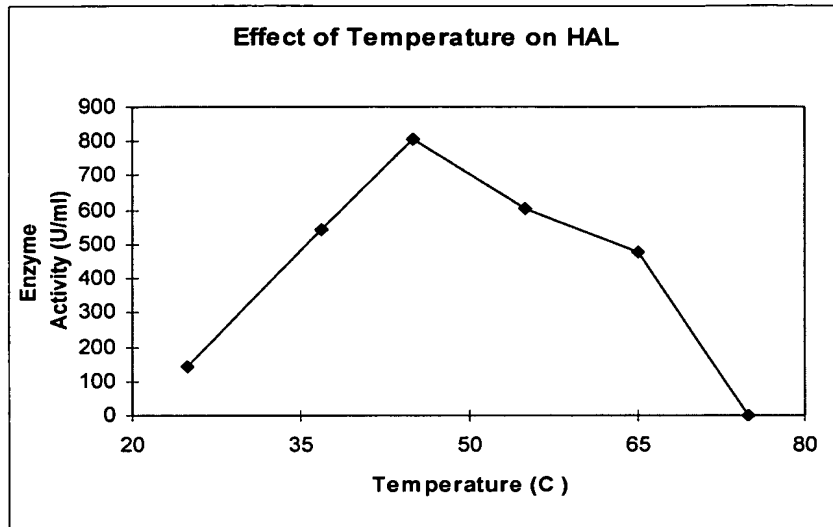


Figure 8: Effect of pH on HAL.

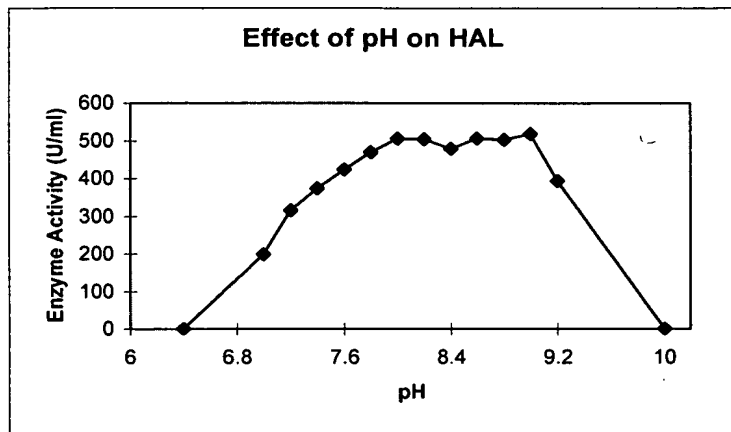


Figure 9: Effect of HAL and Histidinol on HSV.

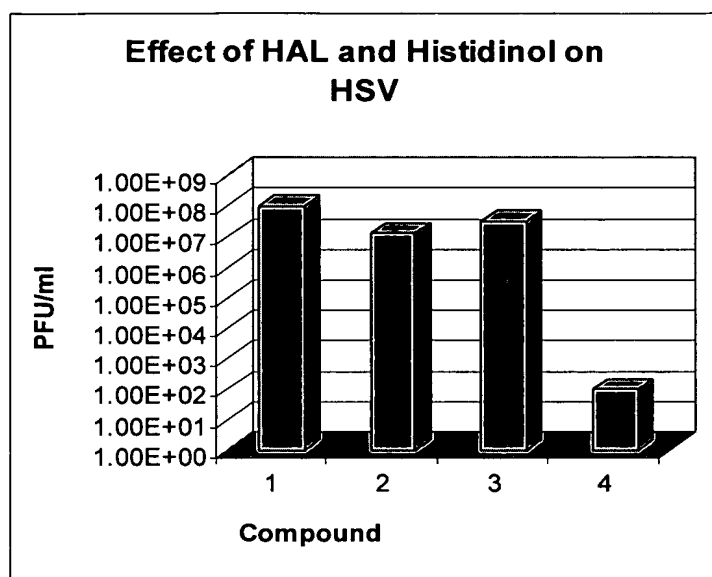


Figure 10: Effectiveness of L-histidinol as a Single Agent

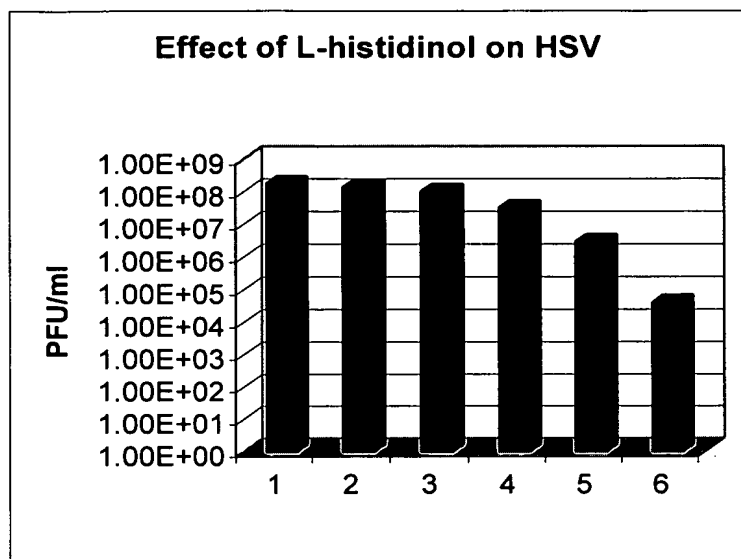


Figure 11: Effect of HAL and Histidinol on RSV.

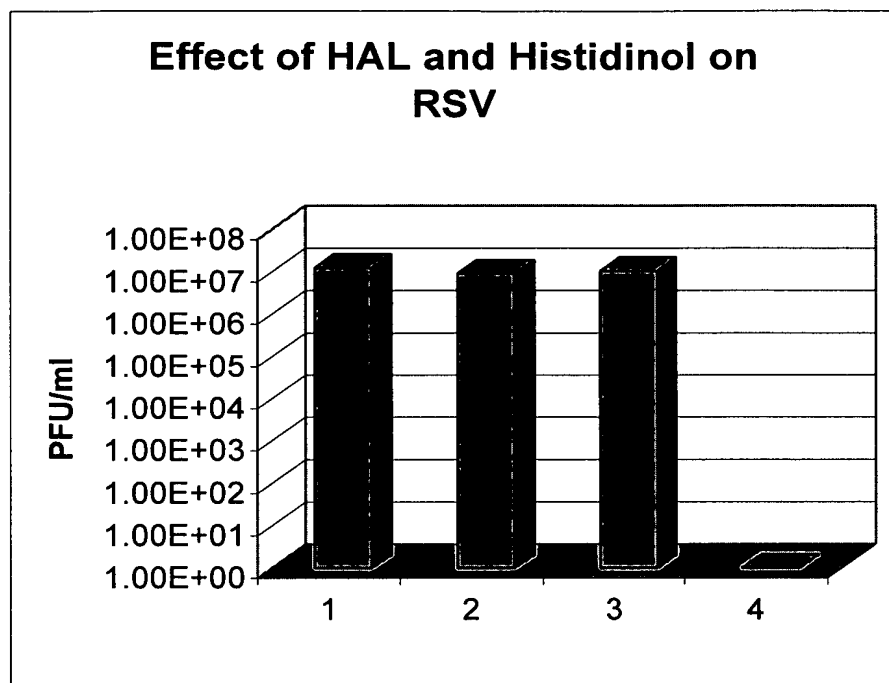


Figure 12: Effect of HAL on RMuLV.

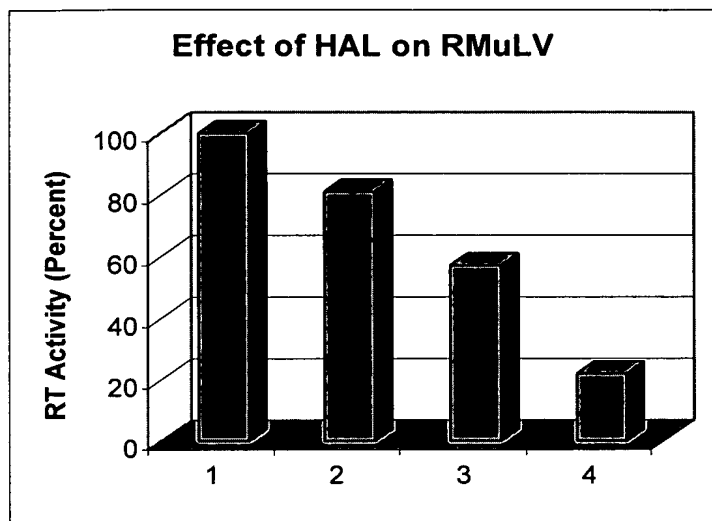


Figure 13A

```

HUTH_PSEPU -----
-
HUTH_RHIME -----
-
HUTH_MOUSE
MPRYTVHVRGEWLAVPCQDGKLTVGWLGREAVRRYMKNKPDNGGFTSVDEVQFLVHRCKG
HUTH_RAT
MPRYTVHVRGEWLAVPCQDGKLSVGWLGREAVRRYMKNKPDNGGFTSVDEVFLVRRCKG
HUTH_HUMAN
MPRYTVHVRGEWLAVPCQDAQLTVGWLGREAVRRYIKNKPDNGGFTSVDDAHFLVRRCKG
HUTH_CAEEL -MRLQVQIGTECVVVPCKP-DDTIHAVAKKSVEKLRRLRPK----
LPLADDYFEVRRTVG
HUTH_BACS -----
-
HUTH_STRGR -----
-
HUTH_CORY -----
-

HUTH_PSEPU -----
-
HUTH_RHIME -----
-
HUTH_MOUSE LGLLDNEDELEVALEDNEFVEVVIEGDVMS-----PDFIPSQPEGVFLYSKYR---
-
HUTH_RAT LGLLDNEDLLEVALEDNEFVEVVIEGDVMS-----PDFIPSQPEGVFLYSKYR---
-
HUTH_HUMAN LGLLDNEDRLEVALENNEFVEVVIEGDAMS-----PDFIPSQPEGVFLYSKYR---
-
HUTH_CAEEL
NSLLDPEDLVSDVLKDSDFIIVAASVEETEDAKEAKKQEEIDNARAEIEKIDNRRRKVSF
HUTH_BACS -----
-
HUTH_STRGR -----
-
HUTH_CORY -----
-

HUTH_PSEPU -----
TELTLKPGTLTLAQLRAIHAAPVRLQLDASAAPIDASVACVEQIIA
HUTH_RHIME -----
MTVILRPGSVPLSDLETIYWTGAPARLDAAFDAGIAKAAARIAEIVA
HUTH_MOUSE -----
EPEKYIALDGDLSLSTEDLVNLGKGGRYKIKLTSIAEKKVQQSREVIDSIK
HUTH_RAT -----
EPEKYIALDGDLSLSTEDLVNLGKGGRYKIKLTSIAEKKVQQSREVIDSIK
HUTH_HUMAN -----
EPEKYIELDGDRLTEDLVNLGKGGRYKIKLTPAEKRVQKSREVIDSIK
HUTH_CAEEL
ADSLAPMVLAPPTKLLILDGNSLLPEDLVRCEKGECAIQLSMESEDRIRKARTFLEKIAS
HUTH_BACS -----
MVTLDGSSLTTADVAVRLFDFEEAAASEESMERVKKSRAAVERIVR
HUTH_STRGR -----
MDMHTVVVGTSGTTAEDVVAVARHGARVELSAAAVEALAAARLIVDALAA
HUTH_CORY -----
MASAPQITLGLSGATADDVIAVARHEARISISPVLEELASVRAHIDALAS

```

Figure 13B

HUTH_PSEPU
EDRTAYGINTGFGLLASTRIASHDLENLQ RSLVLSHAAGIGAPLDDDLVRLIMVLKINSL
HUTH_RHIME
GNAPVYGINTGFGKLASIKIDSSDVATLQRNLILSHCCGVGQPLTEDIVRLIMALKLISL
HUTH_MOUSE
ERTVVYGITTGFGKFARTVIPANKLQELQVNLVRSHSSGVGKPLSPERCRMLLALRINVL
HUTH_RAT
ERTVVYGITTGFGKFARTVIPANKLQELQVNLVRSHSSGVGKPLSPERCRMLLALRINVL
HUTH_HUMAN
EKTVVYGITTGFGKFARTVIPINKLQELQVNLVRSHSSGVGKPLSPERCRMLLALRINVL
HUTH_CAEEL
EHRVYGVTTGFGTFSNVTIPPEKLLKQLNLIRSHATGYGEPLAPNRARMMLLALRINIL
HUTH_BACS
DEKTIYGINTGFGKFSDVLIQKEDSAALQNLILSHACGVGDPFPECVSRAMLLLRANAL
HUTH_STRGR
KPEPVYGVSTGFGALASRHIGTELRAQLQRNIVRSHAAGMGPVEREVVRALMFLRLKTV
HUTH_CORY
ADTPVYGISTGFGALATRHIAPEDRAKLQRSLIRSHAAGMGEPVEREVVRALMFLRAKTL

HUTH_PSEPU
SRGFSGIRRKVIDALIALVNAEVYPHIPKGSVGASGDLAPLATMSLVLLGEGKARYKGO
HUTH_RHIME
GRGASGVRLELVRLIEAMLDKGVIPLIPEKGSVGASGDLAPLAHMAAVMMGHGEAFFAGE
HUTH_MOUSE
AKGYSGISLETCLKQVIEAFNASCLSYVPEKGTVGASGDLAPLSHLALGLIGEGKMWSPKS
HUTH_RAT
AKGYSGISLETCLKQVIEVFNASCLSYVPEKGTVGASGDLAPLSHLALGLIGEGKMWSPKS
HUTH_HUMAN
AKGYSGISLETCLKQVIEMFNASCLPYVPEKGTVGASGDLAPLSHLALGLVGEKGMWSPKS
HUTH_CAEEL
AKGHSGISVENIKKMIAAFNAFCVSYPVQQGTGCSGDLCPLAHLALGLLGEKGMWSPTT
HUTH_BACS
LKGFSGVRAELIEQLLAFLNKRVPVIPPQQGSLGASGDLAPLSHLALALIGQGEVFFEGE
HUTH_STRGR
ASGHTGVRPEVAQTMADVNLNAGITPVVHEYGSLGCSGDLAPLSHCALTMGEGEAEAGPDG
HUTH_CORY ASGRS-
VRPVVLETMVGMNLNAGITPVVREYGSLGCSGDLAPLSHCALVLMGEGEATDAHG

HUTH_PSEPU -
WLSATEALAVAGLEPLTLAAKEGLALLNGTQASTAYALRGLFYAEDLYAAAIACGGLSV
HUTH_RHIME -
RMKGDAALKAAGLSPVTLAAKEGLALINGTQVSTALALAGLFRAHRAGQAALITGALST
HUTH_MOUSE
GWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITS LGCEALERASAIARQADIVAALT
HUTH_RAT
GWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITS LGCEAVERASAIARQADIVAALT
HUTH_HUMAN
GWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITS LGCEAVERASAIARQADIVAALT
HUTH_CAEEL
GWQPADVVLKKNLEPLELGPKEGLALINGTQMVTALGAYTLERAHNIARQADVIAALS
HUTH_BACS -
RMPAMTGLKKAGIQPVTLT SKEGLALINGTQAMTAMGVVAYIEAEKLAYQTERIASLTI
HUTH_STRGR
TVRPAGELLAHGIAPVELREKEGLALLNGTDGMLGMLVMALADLRNLYTSADITAALS
HUTH_CORY
DIRPVPELFAEAGLTPVELAEKEGLALVNGTDGMLGQLIMALADLDELDDIADATAAMSV

Figure 13C

HUTH_PSEPU EAVLGSRSPFDARIHE-ARGQRGQIDTAACFRDLLGDSSEVSLSHKNCD----
KVQDPYS
HUTH_RHIME DAAMGSSAPFHPDIQH-CAAIRARSTRAAALRQLLTG-SPIRQSHIEGDE---
RVQDPYC
HUTH_MOUSE EVLKGTTKAFDTDIHA-VRPHRGQIEVAFRFRSLLDS-
DHHPSEIAESHRFCDRVQDAYT
HUTH_RAT EVLKGTTKAFDTDIHA-VRPHRGQIEVAFRFRSLLDS-
DHHPSEIAESHRFCDRVQDAYT
HUTH_HUMAN EVLKGTTKAFDTDIHA-LRPHRGQIEVAFRFRSLLDS-
DHHPSEIAESHRFCDRVQDAYT
HUTH_CAEEL DVLKGTTRAYDPDIHR-IRPHRGQNL SALRLRALLHS-
EANPSQIAESHRNCTKVQDAYT
HUTH_BACS EGLQGIIDAFDEDIHL-ARGYQE QIDVAERIRFYLS- SGLTTSQGE-----
LRVQDAYS
HUTH_STRGR EALLGTDKVLAPELHA-IRPHPGQVSADNMSRVLAG-SGLTGHHQDDAP---
RVQDAYS
HUTH_CORY EAQLGTDQVFRAELHEPLRPHPGQGRSAQNMFAFLAD-SPIVASHREGDG---
RVQDAYS

HUTH_PSEPU
LRCQPQVMGACLTQLRQAAEVLGIEANAVSDNPLVFAAEGDVISGGNFHAEPVAMAADNL
HUTH_RHIME IRCQPQVDGACLDLLRSVAATLTIEANAVTDNPLVLSDN-
SVVSGGNFHAEPVAFADQI
HUTH_MOUSE
LRCCPQVHGVVNDTIAFVKDIITTELNSATDNPMVFASRGETISGGNFHGEYPAKALDYL
HUTH_RAT
LRCCPQVHGVVNDTIAFVKDIITTELNSATDNPMVFASRGETISGGNFHGEYPAKALDYL
HUTH_HUMAN
LRCCPQVHGVVNDTIAFVKNIITTELNSATDNPMVFANRGETVSGGNFHGEYPAKALDYL
HUTH_CAEEL
LRCVPQVHGVVHDTIEFVREIITTEMNSATDNPLVFADREEIISGGNFHGEYPAKALDFL
HUTH_BACS
LRCIPQVHGATWQTLGYVKEKLEIEMNAATDNPLIFNDGDKVISGGNFHGQPIAFAMDFL
HUTH_STRGR VRCAPQVNGAGRDTLDHAALVAGRELASSVDNPFVLPDG-
RVESNGNFHGAPVAYVLDL
HUTH_CORY LRCSQVGTGAARDTIAHARLVATRELAAAIDNPFVLPDG-
EVTISNGNFHGAPVAYVLDL

HUTH_PSEPU ALAIAEIGSLSERRISLMMDKHMS-
QLPPFLVENGGVNSGFMIAQVTAAALASENKALSH
HUTH_RHIME
ALAVCEIGAISQRRIALLVDPALSLRLPAFLAKKPGLN SGLMIAEVTSAALMSENKQLSH
HUTH_MOUSE AIGVHELAAISERRIERLCNP SLS-
ELPAFLVAEGGLNSGFMIAHCTAAALVSESKALCH
HUTH_RAT AIGVHELAAISERRIERLCNP SLS-
ELPAFLVAEGGLNSGFMIAHCTAAALVSESKALCH
HUTH_HUMAN AIGIHELAAISERRIERLCNP SLS-
ELPAFLVAEGGLNSGFMIAHCTAAALVSESKALCH
HUTH_CAEEL AIAVAELAQMSERRRLRLVNKELS-
GLPTFLT PDGGLNSGFMTVQLCAASLVSENKVLCH
HUTH_BACS KIAISELANIAERRIERLVNPQLN-
DLPPFLSPHPGLQSGAMIMQYAAASLVSENKTLAH
HUTH_STRGR
AIVAADLGSICERRTRDRLLDKNRSHGLPPFLADDAGVDSGLMIAQYTQAALVSEMKRLAV
HUTH_CORY
AIAVADLGSIAERRTRDRLDPAFLADDPGVDSGMMIAQYTQAGLVAENKRLAV

Figure 13D

HUTH_PSEPU	PHSVDSLPTSANQEDHVSMAPAAGKRLWEMAENTRGVPAIEWLGACQGLDLRKG-LKTS
HUTH_RHIME	PASVDSTPTSANQEDHVSMACHGARRLLQMTENLFSIIGIEALAAVQGIEFRAP-LTTS
HUTH_MOUSE	PSSVDSLSTSAATEDHVSMGGWAARKALRVVEHVEQVLAIELLAACQGIEFLRP-LKTT
HUTH_RAT	PSSVDSLSTSAATEDHVSMGGWAARKALRVIEHVEQVLAIELLAACQGIEFLRP-LKTT
HUTH_HUMAN	PSSVDSLSTSAATEDHVSMGGWAARKALRVIEHVEQVLAIELLAACQGIEFLRP-LKTT
HUTH_CAEEL	PSSVDSIPTSCNQEDHVSMGGFAARKALTVEHVEAVLAMELLAACQGIEFLKP-LIST
HUTH_BACS	PASVDSIPSSANQEDHVSMGTIAARHAYQVIANTRRVIAIEAICALQAVEYRGI-EHAA
HUTH_STRGR	
PASADSIPSSAMQEDHVSMGWSAARKLRTAVDNLARIVAVELYAATRAIELRAAEGLTPA	
HUTH_CORY	PA-VDSIPSSAMQEDHVSLGWHAARKLPTSVANLRRILAVEMLIAGRALDLRAP-LKPG
HUTH_PSEPU	AKLEKARQALRSEVA-HYDRDRFFAPDIEKAVELLAKG---S-LTGLLPAGVLPSSL---
-	
HUTH_RHIME	PELQKAAAVRGVSS-SIEEDRYMADDLKAAGDLVASG---R-LAAVSAGILPKLEN-
HUTH_MOUSE	TPLEKVYDLVRSVVR-
PWIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEKYRMEHIPESR	
HUTH_RAT	TPLEKVYDLVRSVVR-
PWIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEKYRMEHIPESR	
HUTH_HUMAN	TPLEKVYDLVRSVVR-
PWIKDRFMAPDIEAAHRLLEQKVWEVAAPYIEKYRMEHIPESR	
HUTH_CAEEL	APLHKIYQLVRSVAP-
PLNEDRYMKPEIDAVLEMIRENRIWEAVLPHLETLEAMEELDPD	
HUTH_BACS	SYTKQLFQEMRKVVP-SIQQDRVFSYDIERLTDWLKK----ESLIPDHQNKELRGMNI-
HUTH_STRGR	PASEAVVAALRAAGAEGPGPDRFLAPDLAAADTFVREG---R-LVAAVEPVTGPLA---
-	
HUTH_CORY	PATGAVLEVLRSKVA-GPGQDRFLSAELEAAAYDLLANG---S-VHKALEAHLPE-----
-	
HUTH_PSEPU	-----
HUTH_RHIME	-----
HUTH_MOUSE	PLSPTAFSLES LRKNSATIPESDDL----
HUTH_RAT	PLSPTAFSLES LRKNSATIPESDDL----
HUTH_HUMAN	PLSPTAFSLQFLHKKSTKIPESEDL----
HUTH_CAEEL	ALRQFTKTPTGIVQDRSMIPISDDEESIE
HUTH_BACS	-----
HUTH_STRGR	-----
HUTH_CORY	-----

Appl. No.: 09/833,745
Inventors: Joseph ROBERTS *et al.*
Atty. Docket No. 078728-0106

Figure 14A

1	983831	100.0%	[MASAPQITLGLSGATADDVI
			AVARHEARISISPOVLEELASVRAHIDALASADTPVYGIS
			STGCFGALATRHIAPEDRAKLQ
1	SWALL: CAC21618	66.1%	---MHTVVVGTSGVTASDVLA
			VARAGARIELSEEAVALAARSVDALA
			AAKPDVPYGVSTGFGALATRHI
			SPELRGRQ
2	SWALL: HUTH_STRGR	65.4%	---MDMHTVVVGTSGTAEVD
			VAVARGARVELSAAAEALAAAR
			LIVDALAAKPEPVYGVSTGFGALASR
			HIQITELRAQLQ
3	SWALL: HUTH_DEIRA	46.8%	-----MILDRINLEQFTSV
			RHGEQVELSAAARERIARATV
			IEQIUEGDTPIYGVNTGFGKFN
			QIDRSQLAQLQ
4	SWALL: BAB16159	42.0%	-----VPLHLHLADIYNN
			GSAKLDPDFDAAVLKGARIAE
			TAAGNAPVYGVNTGFGKLASIK
			IDAADLATLQ
5	SWALL: Q9KWE4	42.0%	-----VPLHLHLADIYNN
			GSAKLDPDFDAAVLKGARIAE
			TAAGNAPVYGVNTGFGKLASIK
			IDAADLATLQ
6	SWALL: HUTH_BACSU	40.4%	-----MVTLDGSSITADV
			ARVLFDFEEAAASEEMERVK
			KSAAVERIVRDEKTIYGIN
			TGFGKFSVDLQKEDS
			SAALQ
7	SWALL: Q9KSQ4	42.2%	-----MLHLMKPGQLSLQ
			RQVSRPVSULDPEAIPAIAE
			SAQVEQVISEGRTVYGIN
			TGFGLLANTKIAPODLE
			TLQ
8	SWALL: Q9HU85	41.7%	-----MSLHLKPGQLTL
			ADLRQAYLAPVRLSLP
			SADAPIAASVACVENIIA
			EGRTAYGINTGFGLLAS
			TRISPADLEKLQ
9	SWALL: Q9KBE6	39.3%	-----MTNLKLLDGRSL
			SLDHLRIIEYEGETV
			GSDESMEKVKQSKRAVEQ
			IIAIDEKIYGITGFGKFS
			DIFIDPDVDENLQ
10	SWALL: HUTH_PSEPU	41.7%	-----TELTLKPGTTLT
			LAQRLAIHAPVRLQD
			ASAAPADAISVACVEQ
			IIAEDRTAYGINTGFGLL
			ASTRIASHDENLQ
11	SWALL: HUTH_RHIME	40.6%	-----LRPGSVPLS
			DLTIYWTGAPARLEDA
			ADFAGIAKAAARIAE
			IVAGNAPVYGIN
			TGFGKLASIKIDSSD
			VAATLQ
12	SWALL: Q9HU90	40.7%	MSDLPSSVYFGDGLPR
			WRQELVAVARGARLES
			AAAWARIDNARAICR
			IVANGERAYGISTG
			GALCDVLLGEGQAL
13	SWALL: HUTH_HUMAN	39.2%	KYREPEKYI
			DLGTTEDLVNLGKGYK
			IKLTPTAERKVQKS
			REVIDSIIEKTVYGI
			TGFGKFA-RTVIPNKLQ
14	SWALL: HUTH_CAEEL	38.8%	VLAPPTKLLILDGNS
			PEDIVRCEKGECALQ
			SMESEDRIKARTF
			LEKTASEHRAVYGT
			TGFGTFSNVTIPEK
			KLKLQ
15	SWALL: Q9HLI6	41.0%	-----MIEDGRSLR
			VEDVAVAYEDRVSI
			ISDDTLKAVEEKHEA
			FLKLSNGKTVYGV
			NTGFGSLLNVHIERQ
			EIELQ
16	SWALL: HUTH_MOUSE	38.6%	KYREPEKYIALD
			GDSTEDLVNLGKGYK
			IKLTSIAEKKVQQS
			REVIDSIIEKTVYGI
			TGFGKFA-RTVIPAN
			KLQLQ
17	SWALL: BAB29407	38.6%	KYREPEKYIALD
			GDSTEDLVNLGKGYK
			IKLTSIAEKKVQQS
			REVIDSIIEKTVYGI
			TGFGKFA-RTVIPAN
			KLQLQ
18	SWALL: HUTH_RAT	38.2%	KYREPEKYIALD
			GDSTEDLVNLGKGYK
			IKLTSIAEKKVQQS
			REVIDSIIEKTVYGI
			TGFGKFA-RTVIPAN
			KLQLQ
19	SWALL: AAG53586	39.8%	-----MNALTLTPGTL
			IAQLRQVWQQPLQTL
			DESAAHEINDSVAC
			VEAIVAEGR
			TAYGINTGFGLLAQ
			TRIAATHDENLQ
20	SWALL: Q9KKE0	38.9%	-----MGEMISLDG
			PLTWREITASIAEG
			ASLDLSPARLRAQ
			ARIVDALVERG
			INGVINTGALCDV
			IISRENQQALS
21	SWALL: Q9HOD5	42.2%	-----MSDTRIDA
			ADREALQ

Figure 14B

983831	100.0%	1	RSLIRSHAAAGGEPVEREVVRALMFLRAKTLASGRGTGRPVVLEMTWGMNLNAGITPVVREYCSGLCSGDLAPLSHCALVL
1 SWALL: CAC21618	66.1%	2	RNIVRSHAAAGGPRVEREVVRALMFLRLKTVCSGRGTGRPEVQTMADVNLNAGITPVVHEYGSLCSGDLAPLSHCALTL
2 SWALL: HUTH_STRGR	65.4%	3	RNIVRSHAAAGGPRVEREVVRALMFLRLKTVASGHTGRPEVQTMADVNLNAGITPVVHEYGSLCSGDLAPLSHCALTL
3 SWALL: HUTH_DEIRA	46.8%	4	HNLIVSHAIGMGEPLPAEVVRGMLLRAQSLSLGSHGVRVEVVELLLALNADALPVVPSQGSVGASGDLAPLAHLALGL
4 SWALL: BAB16159	42.0%	5	RNLILSHCCGVCAPLPENVRRLIMALKLISLGRGASGVRIELIRLIEGMLEKGVIPVPEKGSVGASGDLAPLAHMSATM
5 SWALL: Q9KWE4	42.0%	6	RNLILSHCCGVCAPLPENVRRLIMALKLISLGRGASGVRIELIRLIEGMLEKGVIPVPEKGSVGASGDLAPLAHMSATM
6 SWALL: HUTH_BACSU	40.4%	7	RNLILSHACGVGDPFPECVSRAMLLLRANALLKGFSGVRAELIEQLLAFNKRVRHVPVPOQGSILGASGDLAPLSHLALAL
7 SWALL: Q9KSQ4	42.2%	8	KSIVLSHAAGIGELMSDETVRMLMMLLKINSLARGYSGIRLEVIQALIELVNNQIYPCVPKKGSGVGASGDLAPLAHMSATM
8 SWALL: Q9HU85	41.7%	9	RSIVLSHAAGVGEALDDAMVRVLMKLVNLSLARGFSGIRRKVIDALIALINAEVYPHIPLKGSVGASGDLAPLAHMSLVL
9 SWALL: Q9KBE6	39.3%	10	HNLIVSHACGVGSPFETVSRMTLVIRANALLKGFSGVRPLVIERLLALVNANIHPVPIPOQGSILGASGDLAPLSHLALVL
10 SWALL: HUTH_PSEPU	41.7%	11	RSIVLSHAAGIGCAPLDDIVRLIMVLKINSLRSGFSGIRRKVIDALIALVNAEVYPHIPLKGSVGASGDLAPLAHMSLVL
11 SWALL: HUTH_RHIME	40.6%	12	RNLILSHCCGVCAPLDDIVRLIMALKLISLGRGASGVRLLEVRLEIEMLDKGVIPVPEKGSVGASGDLAPLAHMAAVM
12 SWALL: Q9HU90	40.7%	13	RNTLLSHACGVGEPLRDEQTRAIICAAVANYSQKSGLDRLSVEGLLALNLHGITTQVPAQGSVGY---LTHMAHVGIALL
13 SWALL: HUTH_HUMAN	39.2%	14	VNLVRSHSSGVGKPLSPERCRLMIALRINVLAKYSGISLETILKQVIEFNASCLPVVPEKGTGASGDLAPLSHLALGL
14 SWALL: HUTH_CAEEL	38.8%	15	VNLVRSHSSGVGKPLSPERCRLMIALRINVLAKYSGISLETILKQVIEFNASCLPVVPEKGTGASGDLAPLSHLALGL
15 SWALL: Q9HLI6	41.0%	16	VNLVRSHSSGVGKPLSPERCRLMIALRINVLAKYSGISLETILKQVIEFNASCLPVVPEKGTGASGDLAPLSHLALGL
16 SWALL: HUTH_MOUSE	38.6%	17	VNLVRSHSSGVGKPLSPERCRLMIALRINVLAKYSGISLETILKQVIEFNASCLPVVPEKGTGASGDLAPLSHLALGL
17 SWALL: BAB29407	38.6%	18	VNLVRSHSSGVGKPLSPERCRLMIALRINVLAKYSGISLETILKQVIEFNASCLPVVPEKGTGASGDLAPLSHLALGL
18 SWALL: HUTH_RAT	38.2%	19	VNLVRSHSSGVGKPLSPERCRLMIALRINVLAKYSGISLETILKQVIEFNASCLPVVPEKGTGASGDLAPLSHLALGL
19 SWALL: AAG53586	39.8%	20	RSLVLSHAAGVGEPLDDIVRLMMLKINSLARGFSGIRLSVITQALIALVNAGVYSDVPKGSVGASGDLAPLAHMSLTL
20 SWALL: Q9KKE0	38.9%	21	RNLILSHACGVGDPPLGRVEARAVMAAQIANLTHGYSGRVRETAEMLLALNADIIPVPSRGSVGY-----LTHAALVL
21 SWALL: Q9HQD5	42.2%		ANLIVRSHAAAGGSELDTAAVRALLIVTRLNALAKYSGIRERVLVDVLVGLINEGVHPVVPVPSRGSILGASGDLAPLAHMSRVL

Figure 14C

[illegible]

Figure 14D

	983831	241	320
1	SWALL: CAC21618	100.0%	FRAELHEPLRPHPGQGRSAQNMFALADSPIVASHREGDGRVQDAYSLRCSPOVTGAARDTIAHARLVATRELAALDNP
2	SWALL: HUTH_STRGR	66.1%	LAPELHA-IRPHPGQASAAANMAVLKSGLTGHQDAPRVQDAYSVRCAPQVAGAGRTDMAHAGLVARELAALDNP
3	SWALL: HUTH_DEIRA	65.4%	LAPELHA-IRPHPGQGVADNMVRSLAGSLTGHQDAPRVQDAYSVRCAPQVAGAGRTDLHAALVAGRELASSVDNP
4	SWALL: BAB16159	46.8%	FQPDV-VGLRPHGALAAELREFLAGSETAPSHLTGDGKVQDAYSLRCPQVHGATWDALQAQERVLAVEFASVTDNP
5	SWALL: Q9KWE4	42.0%	FHPDIHT-LRGHKQIDAGSALRNLLQSGSEIRSHIEGDERVQDPYCIRCPQVQDGAACLDLLASVARTLEIEANAVTDNP
6	SWALL: HUTH_BACSU	42.0%	FHPDIHT-LRGHKQIDAGSALRNLLQSGSEIRSHIEGDERVQDPYCIRCPQVQDGAACLDLLASVARTLEIEANAVTDNP
7	SWALL: Q9KSQ4	40.4%	FDEDIHLA-RGYQEQIDVAERIRFYLSDSLTS--QGEIRVQDAYSLRCPQVHGATWQTLGYVKEKLEIEMNAATDNP
8	SWALL: Q9HU85	42.2%	FDPRIHR-VRGHRTQMDAATAYRHLLVSSEIGQSHNCE-KVQDPYSLRCPQVMGACLOQIRSAAEVLEVEANSVSDNP
9	SWALL: Q9KBE6	41.7%	FDARIHAA-RGQRGQIDVAAAAYRDLLASSEVARSHKCD-KVQDPYSLRCPQVMGACLTQMRQAAEVLEIEANAVSDNP
10	SWALL: HUTH_PSEPU	39.3%	FDEQIHFA-RGYVEQVDVARRMESYLQDSQLTT--RQGEIRVQDAYSLRCPQVHGATWQTLRYVKEKLEIEMNAATDNP
11	SWALL: HUTH_RHIME	41.7%	FDARIHAA-RGQRGQIDVAAAAYRDLLASSEVARSHKCD-KVQDPYSLRCPQVMGACLTQMRQAAEVLEIEANAVSDNP
12	SWALL: Q9HU90	40.6%	FHPDIHCAATRARSTRAAA-LRQLTGSPTRQSHIEGDERVQDPYCIRCPQVQDGAACLDLLASVARTLEIEANAVTDNP
13	SWALL: HUTH_HUMAN	40.7%	FDAEI-VALKHPGMQVAAANLRALLAGSVLENAR--GIRTDALSIRSIPIQIHGACRDQLAHARQIET-ELNSATDNP
14	SWALL: HUTH_CAEEL	39.2%	FDTDIHA-LRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGAVNDTIAFVKDIIITELNSATDNP
15	SWALL: Q9HLI6	38.8%	YDPDIHR-IRPHRGQNLALRLALLNPQIAESHRNCT-KVQDAYTLRCPQVHGAVNDTIEFVREIITTEMNSATDNP
16	SWALL: HUTH_MOUSE	41.0%	FTPWILGA-REHLGQVAGNRFRFYLTSGLDIV--KRADSVKVQDAYTLRCPQVHGAVNDTIAFVKDIIITELNSATDNP
17	SWALL: BAB29407	38.6%	FDTDIHA-VRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGAVNDTIAFVKDIIITELNSATDNP
18	SWALL: HUTH_RAT	38.2%	FDTDIHA-VRPHRGQIEVAFRFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGAVNDTIAFVKDIIITELNSATDNP
19	SWALL: AAG53586	39.8%	FDARIHE-VRQGRGQIDAAALFRHVLTDTSIAIAASHNCD-KVQDPYSLRCPQVMGACLTQMRQAAEVLLVESNAVSDNP
20	SWALL: Q9KKE0	38.9%	AFaelPLALRQSPGLSAGEGLRWLADSPMLAG--TAGTRTQDPLSLRAVPQVHGAAARDAFGQVAEIVDRELASVTDNP
21	SWALL: Q9HQD5	42.2%	CAPAIHE-VRPHDGQAVSARHIRNLTAGSEVLDHHRDCCD-RVQDAYSLRCLPQVHGAVRDALDHLRAAVATELNSATDNP

Figure 14E

983831	100.0%	[VVLPSEVTSGNGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	400
1 SWALL: CAC21618	66.1%		VVLPDGRVESNGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
2 SWALL: HUTH_STRGR	65.4%		VVLPDGRVESNGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
3 SWALL: HUTH_DEIRA	46.8%		LIFPTGEVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
4 SWALL: BAB16159	42.0%		LVLSDNSVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
5 SWALL: Q9KWE4	42.0%		LVLSDNSVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
6 SWALL: HUTH_BACSU	40.4%		LIFNDGDVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
7 SWALL: Q9KSQ4	42.2%		LVFADGDVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
8 SWALL: Q9HU85	41.7%		LVFADGDVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
9 SWALL: Q9KBE6	39.3%		LIFDNGQVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
10 SWALL: HUTH_PSEPU	41.7%		LVFADGDVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
11 SWALL: HUTH_RHIME	40.6%		LVLSDNSVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
12 SWALL: Q9HU90	40.7%		LLLGTPPEVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
13 SWALL: HUTH_HUMAN	39.2%		MVFANGETVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
14 SWALL: HUTH_CAEEL	38.8%		LVFADREIISGNGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
15 SWALL: Q9HLI6	41.0%		L-FNGEEVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
16 SWALL: HUTH_MOUSE	38.6%		MVFASGETISGNGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
17 SWALL: BAB29407	38.6%		MVFASGETISGNGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
18 SWALL: HUTH_RAT	38.2%		MVFASGETISGNGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
19 SWALL: AAG53586	39.8%		LVFANEMVFRGNGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
20 SWALL: Q9KKE0	38.9%		AVAGSPEVHSQAHAVGAALGLAMDSIAVAVAEVAAISERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	
21 SWALL: Q9HQD5	42.2%		LVPSPGTVSVSGNFHGPVAYVLDLAVADLGSIAERRTRDMLDPAERSRDLPAFLADDPGVDSGMIAQYTQAGLVAE	

[illegible]

Figure 14G

	983831	481	[. . . 5] 513
1	SWALL: CAC21618	100.0%	PGQDRFLSAEIEAAYDLLANGSVHKALEAHLPA
2	SWALL: HUTH_STRGR	66.1%	PGPDRHLAPDLAAADAFVRAGHLVAAAESVTGP
3	SWALL: HUTH_DEIRA	65.4%	PGPDRFLAPDLAAADTFVREGRLVAAVEPVTGP
4	SWALL: BAB16159	46.8%	LTEDRYFRPDLRLRGEIVSGRVAQAADTQAPA
5	SWALL: Q9KWE4	42.0%	LEDDRYMATDLKAAIEVVASGALVSAISSGLPV
6	SWALL: HUTH_BACSU	42.0%	LEDDRYMATDLKAAIEVVASGALVSAISSGLPV
7	SWALL: Q9KSQ4	40.4%	IQQDRVFSYDIERLTDWLKESLIPDHQNKELR
8	SWALL: Q9HU85	42.2%	YDKDRYFAPDIEKANALL-QLAVHNRLMPDQLL
9	SWALL: Q9KBE6	41.7%	YQEDRFAPDIEAASQLLASGCLNALLPARLLP
10	SWALL: HUTH_PSEPU	39.3%	IDQDRMFAKDIERAAKWLKDGSDFTKMKREKER
11	SWALL: HUTH_RHIME	41.7%	YDRDRFFAPDIEKAVELLAKGSLTGLLPAGLPS
12	SWALL: Q9HU90	40.6%	IEEDRYMADDLKAAGDLVASGRLAASVAGLPK
13	SWALL: HUTH_HUMAN	40.7%	YDTRWLAPDIASAAAILGERKSLARLAASIGD
14	SWALL: HUTH_CAEEL	39.2%	WIKDRFMAPDIEAAHRLLEQKVWEVAAAPYIEK
15	SWALL: Q9HLI6	38.8%	PNEDRYMKPEIDAVLEMTIRENRIWEAVLPHELE
16	SWALL: HUTH_MOUSE	41.0%	LDHDPSPSFDIETIRKMDKKEFTSALP-----
17	SWALL: BAB29407	38.6%	WIKDRFMAPDIEAAHRLLLDQKVWEVAAAPYIEK
18	SWALL: HUTH_RAT	38.6%	WIKDRFMAPDIEAAHRLLLDQKVWEVAAAPYIEK
19	SWALL: AAG53586	38.2%	WIKDRFMAPDIEAAHRLLLDQKVWEVAAAPYIEK
20	SWALL: Q9KKE0	39.8%	YDDDRFFAPDIEAAISLNLKGSGLVGLLPAFL--
21	SWALL: Q9HQD5	38.9%	PIATIVR-----
		42.2%	PAGDRALADDMAAVGDLVRAGLVEDAVARALDA

Figure 14H

KEY:

983831 : HAL

1	CAC21618	: Streptomyces coelicolor
2	HUTH_STRGR	: Streptomyces griseus
3	HUTH_DEIRA	: Deinococcus radiodurans
4	BAB16159	: Agrobacterium rhizogenes
5	Q9KWE4	: Agrobacterium rhizogenes
6	HUTH_BACSU	: Bacillus subtilis
7	Q9KSQ4	: Vibrio cholerae
8	Q9HU85	: Pseudomonas aeruginosa
9	Q9KBE6	: Bacillus halodurans
10	HUTH_PSEPU	: Pseudomonas putida
11	HUTH_RHIME	: Rhizobium meliloti
12	Q9HU90	: Pseudomonas aeruginosa
13	HUTH_HUMAN	: Human
14	HUTH_CAEEL	: Caenorhabditis elegans
15	Q9HLI6	: Thermoplasma acidophilum
16	HUTH_MOUSE	: Mouse
17	BAB29407	: Mus musculus (Mouse)
18	HUTH_RAT	: Rat
18	AAG53586	: uncultured bacterium pCosAS1
20	Q9KKE0	: Rhizobium meliloti
21	Q9HQD5	: Halobacterium sp

Figure 15A

STRG	6	VVVGTSGTTAEDVVAVARHGARVELSAAAVEALAAARLIVDALAAKPEPVYGVSTGFAL	
"HAL"	7	ITLGLSGATADDVIAVARHEARISISPPQVLEELASVRAHIDALASADTPVYGISTGFAL	
		* * * * *	* * * * *
STRG,	66	ASRHIGTELRAQLQRNIVRSHAAGMPRVEREVVRALMFLRLKTVASGHTGVRPEVAQTM	
HAL	67	ATHIAPEDRAKLQRSIRSHAAGMGEPPEREVVRALMFLRAKTLASGRTGVRPVLVETM	
		* * * * *	* * * * *
STRG	126	ADVLNAGITPVVHEYGSLGCSGDLAPLSHCALTLMGEAGEGPDGTVRPAGELLAAHGIA	
HAL	127	VGMLNAGITPVVREYGSLGCSGDLAPLSHCALVLMGEGEATDAHGDIRPVPELFAEAGLT	
		* * * * *	* * * * *
STRG	186	PVELREKEGLALLNGTDGMLGMLVMALADLRNLYTSADITAAALSLEALLGTDKVLAPELH	
HAL	187	PVELAEKEGLALVNGTDGMLGQLIMALADLDELDDIADATAAMSVEAQLGTDQVFRAELH	
		* * * * *	* * * * *
STRG	246	A-IRPHPGQGSADNMSRVLAGSLTGHHQDDAPRVQDAYSVRCAPQVNGAGRDTLDHAA	
HAL	247	EPLRPHPGQGRSAQNMFAFLADSPIVASHREGDGRVQDAYSLRCSQVVTGAARDTIAHAR	
		* * * * *	* * * * *
STRG	305	LVAGRELASSVDNPVLPDGRVESNGNFHGAPVAYVLDFLAIVAADLGSICERRTRDLLD	
HAL	307	LVATRELAAAIDNPVLPSPGEVTSNGNFHGAPVAYVLDFLAIAVADLGSIAERRTRDMLD	
		* * * * *	* * * * *

Figure 15B

STRG	365	KNRSHGLPPFLADDAGVDSGLMIAQYTQAALVSEMKRRLAVPASADSI	IPSSAMQEDHVS	MG
HAL	367	PARSRDLPAFLADDDPGVDSGMMIAQYTQAGLVAENKRRLAVPASVDSI	IPSSAMQEDHVS	LG
		** ** *	** ** *	** ** *
STRG	425	WSAARKLRTAVDNLARIVAVELYAATRAIELRAAEGLTPAPASEAVVAALRAAG	EGPGP	
HAL	427	WHAARKLRTSVANLRRILAVEMLIAGRALDLRAP--LKPGPATGAVLEVLRSKVA	-GPGQ	
		* ** *	* ** *	* ** *
STRG	485	DRFLAPDLAAADTFVREGRLVA	AVE	
HAL	484	DRFLSAELEAAAYDLLANGSVHKA	LE	
		***	*	*